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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/081,737	05/19/98	LIU	19959Y

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EXAMINER	
TUNG,P	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/081,737	Applicant(s) Liu et al.
	Examiner Peter Tung	Group Art Unit 1652

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-48* is/are pending in the application.

Of the above, claim(s) *13-15, 32-34, and 39-48* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *2, 3, 10-12, 17, 18, 20-31, and 35-38* is/are rejected.

☒ Claim(s) *1, 4-9, 16, and 19* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12, 16-31 and 35-38, drawn to DNA encoding uncoupling protein 3, transformed host cells and a method of making uncoupling protein 3, classified in class 435, subclass 69.1.

II. Claims 13-15, 32-34 and 45-48, drawn to uncoupling protein 3 and compositions, classified in class 530, subclass 350.

III. Claims 39-43, drawn to a method of identifying a modulator of uncoupling protein 3 activity, classified in class 435, subclass 4.

IV. Claim 44, drawn to a method of DNA cloning, classified in class 435, subclass 91.1.

2. The inventions are distinct, each from the other because of the following reasons: Inventions of Group I and Group II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product can be made by a different process such as by peptide synthesis.

3. Each of groups I, III and IV is directed to a separate and distinct invention. Group I is directed to a method of making uncoupling protein 3, Group II is directed to a method of identifying a modulator of uncoupling protein 3 and Group IV is directed to a method of DNA cloning. These methods are distinct both physically and functionally, require different process steps, reagents and parameters and produce different products.

4. Each of groups I and II is directed to a separate and distinct invention. Group I is directed to DNA encoding uncoupling protein 3 and transformed hosts while Group II is directed toward uncoupling protein 3.

The products of Group I and II would be expected to have distinct morphological, functional, chemical and physical properties as indicated by their divergent classification, process of making and process of using. These products are capable of separate manufacture, use, or sale as claimed, and are patentably distinct.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

6. During a telephone conversation with Dr. Mark Hand on 12/4/98 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-12, 16-31 and 35-38. Affirmation of this election must be made by applicant in replying to this Office action. Claims 13-15, 32-34 and 39-48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claim Objections

8. Claims 1, 3, 16, 17, 20, 22, 35 and 36 are objected to because of the following informalities: Nucleotide and amino acid sequences are included in the claims. Appropriate correction is required.

9. Claim 36 is objected to because of the following informalities: "... encodes a protein consists of the amino acid..." is incorrect. Appropriate correction is required.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 10-12, 18, 29-31 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. The term "overexpressed" in claims 10-12 and 29-31 is a relative term which renders the claim indefinite. The term "overexpressed" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The uncoupling protein 3 is supposed to be overexpressed from the same host cell and vector that expresses uncoupling protein 3. There is no indication of what levels of protein expression would be meant by "overexpressed."

13. Claims 18 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: and isolating the expressed protein.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

15. Claims 3 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Boss et al. (cited in IDS). Boss et al. teach a cDNA encoding a protein consisting of the sequence of SEQ ID NO:12 (page 40, last paragraph, lines 1-7; Figure 1), which is that of the instant claim.

16. Claims 21, 22 and 36 rejected under 35 U.S.C. 102(a) as being anticipated by Sanchis et al. with evidence by Naeve et al. Sanchis et al. is prior art because SEQ ID NO: 17 and 18 are first disclosed in Provisional application No. 60/069,141, filed 12/9/97.

With regard to claim 21, Sanchis et al. teach a DNA identical, except for a one nucleotide mismatch, to the DNA comprising nucleotides 211 to 1137 of SEQ ID NO: 17 (MasPar Search using the Smith-Waterman algorithm with a default TABLE and Gap of 6). A one nucleotide mismatch out of 927 nucleotides gives a sequencing error rate of 0.11%, well below the error rate of 1-2% obtained with automated sequencing, as taught by Naeve et al. (page 448, page 452, last column, 2nd paragraph, lines 1-4). Therefore claim 21 is anticipated by Sanchis et al. with evidence by Naeve et al.

With regard to claims 22 and 36, Sanchis et al. teach a DNA which encodes a protein consisting of a sequence identical to SEQ ID NO: 18 (coding sequence consisting of nucleotides 165-1091 of the 1357 nucleotide DNA), which is that of the instant claims.

17. Claims 20 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Zhang et al. with evidence by Naeve et al.

With regard to claim 20, Zhang et al. teach a DNA identical, except for a 10 nucleotide mismatch, to the DNA comprising SEQ ID NO: 17 (MasPar Search using the Smith-Waterman algorithm with a default TABLE and Gap of 6) (Columns 5-10, SEQ ID NO: 1). A 10 nucleotide mismatch out of 1,628 nucleotides gives a sequencing error rate of 0.61%, well below the error rate of 1-2% obtained with automated sequencing, as taught by Naeve et al. (page 448, page 452,

last column, 2nd paragraph, lines 1-4). Therefore claim 20 is anticipated by Zhang et al. with evidence by Naeve et al.

With regard to claim 21, Zhang et al. teach a DNA identical, except for a one nucleotide mismatch, to the DNA comprising nucleotides 211 to 1137 of SEQ ID NO: 17 (MasPar Search using the Smith-Waterman algorithm with a default TABLE and Gap of 6) (Columns 5-10, SEQ ID NO: 1). A one nucleotide mismatch out of 927 nucleotides gives a sequencing error rate of 0.11%, well below the error rate of 1-2% obtained with automated sequencing, as taught by Naeve et al. (page 448, page 452, last column, 2nd paragraph, lines 1-4). Therefore claim 21 is anticipated by Zhang et al. with evidence by Naeve et al.

18. Claim 22 is rejected under 35 U.S.C. 102(e) as being anticipated by Zhang et al. Zhang et al. teach a DNA encoding a mouse uncoupling protein 3 which comprises the amino sequence of SEQ ID NO: 18 (column 17, claim 1; columns 13-16, SEQ ID NO:4), which is that of the instant claim.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boss et al. (cited in IDS) in view of Lee et al. Boss et al. teach the complete amino acid sequence of uncoupling protein 3 (UCP3), which is the predicted sequence of human UCP3 cDNA (page 40, last paragraph). Boss et al. do not teach the sequence of the cDNA encoding the human UCP3. Lee et al. teach the isolation of the full length cDNA encoding a porcine enzyme by sequencing the N-terminus of the purified enzyme, using this information to produce degenerate oligonucleotide primers, generating a cDNA probe by polymerase chain reaction amplification of porcine mRNA using the oligonucleotide probes and using the cDNA probe to screen a porcine lambda cDNA library to obtain the full-length cDNA encoding the enzyme (page 1289, column 2, 2nd paragraph - page 1290, 1st paragraph; page 1289, Figure 1). Lee et al. do not teach DNA encoding human UCP3. It would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate the full length cDNA encoding UCP3 by the method of Lee et al., using the amino acid sequence of UCP3, as taught by Boss et al. One of ordinary skill in the art is motivated to obtain the DNA encoding UCP3 in order to help characterize an important metabolic carrier protein. One of ordinary skill in the art has a reasonable expectation of obtaining the DNA encoding UCP3 because the method taught by Lee et al. would be expected to work for any protein where the amino acid sequence is known, and the entire amino acid sequence of human UCP3 is taught by Boss et al. Because nucleotides 344 to 1282 of SEQ ID NO: 11 encode the protein of SEQ ID NO:12 and Boss et al. teach the sequence of SEQ ID NO:12, it would be a reasonable expectation to obtain the DNA sequence consisting of nucleotides 344 to

1282 of SEQ ID NO: 11. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

21. Claims 23, 26, 29, 37 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. with evidence by Naeve et al. The teachings of Zhang et al. with evidence by Naeve et al. have been discussed *supra*. Zhang et al. also teach making mouse uncoupling protein 3 by expressing polypeptide from DNA introduced into a host cell and isolating the expressed polypeptide (column 3, lines 1-9). It would have been obvious to one of ordinary skill in the art at the time the invention was made to transform a host cell with a vector containing DNA encoding mouse uncoupling protein 3, incubating the host cell under conditions to allow expression of the polypeptide from the DNA and isolating the polypeptide. A person of ordinary skill in the art is motivated to do this in order to produce mouse uncoupling protein 3. One of ordinary skill in the art has a reasonable expectation of success at doing this because it is a reasonable expectation to be able to construct a vector containing mouse uncoupling protein 3, transform a host cell with the DNA, grow the cells and isolate the expressed protein, as this is also well known in the art. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

22. Claims 24, 27 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. with evidence by Naeve et al., in view of Scorer et al. The teachings of Zhang et al. with evidence by Naeve et al. have been discussed *supra*. Zhang et al. with evidence by Naeve et al. do not teach the use of a eukaryotic expression vector. Scorer et al. teach the use of yeast

expression vectors for the expression of foreign genes in yeast (page 182, Figure 1; page 183-184, "Experimental Protocol," entire section). Scorer et al. do not teach mouse uncoupling protein 3. It would have been obvious to one of ordinary skill in the art at the time the invention was made to transform a yeast host cell with an expression vector, as taught by Scorer et al., containing DNA encoding mouse uncoupling protein 3 as taught by Zhang et al. with evidence by Naeve et al. and to express the protein. A person of ordinary skill in the art is motivated to do this for the benefit of producing large amounts of uncoupling protein 3. A person of ordinary skill in the art has a reasonable expectation of success at making an expression vector containing the UCP3 DNA, transforming yeast, and producing protein since Scorer et al. teach this using the HIV ENV gene. It would be a reasonable expectation that the DNA encoding UCP3 can be similarly constructed into a vector and expressed. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

23. Claims 25, 28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. with evidence by Naeve et al., in view of Studier et al. The teachings of Zhang et al. with evidence by Naeve et al. have been discussed *supra*. Zhang et al. with evidence by Naeve et al. do not teach the use of a procaryotic expression vector. Studier et al. teach the use of bacterial expression vectors for the expression of foreign genes in *E. coli* (page 113, Abstract). Studier et al. do not teach mouse uncoupling protein 3. It would have been obvious to one of ordinary skill in the art at the time the invention was made to transform *E. coli* with an expression vector, as taught by Scorer et al., containing DNA encoding mouse uncoupling protein 3 as taught by Zhang

et al. with evidence by Naeve et al. and to express the protein. A person of ordinary skill in the art is motivated to do this for the benefit of producing large amounts of uncoupling protein 3. A person of ordinary skill in the art has a reasonable expectation of success at making an expression vector containing the UCP3 DNA, transforming *E. coli* and producing protein since Studier et al. teach that their system can be used with almost any gene. It would be a reasonable expectation that the DNA encoding UCP3 can be similarly constructed into a vector and expressed. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

24. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. with evidence by Naeve et al. The teachings of Zhang et al. with evidence by Naeve et al. have been discussed *supra*. Additionally, Zhang et al. teach that this DNA encodes a mouse uncoupling protein 3 (column 2, lines 4-11). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the DNA as taught by Zhang et al. A person of skill in the art is motivated to do this in order to obtain DNA encoding a mouse uncoupling protein 3. A person of ordinary skill in the art has a reasonable expectation of success at doing this because the DNA sequence is taught by Zhang et al. While Zhang et al. with evidence by Naeve et al. teach a DNA comprising the DNA of SEQ ID NO: 17 but not consisting of SEQ ID NO:17, the two DNAs are not patentably distinct. Both DNAs encode the same mouse uncoupling protein 3 and there is no evidence that the sequence consisting of SEQ ID NO: 17 would express mouse uncoupling protein 3 differently than that taught by the prior art. Therefore the invention as a

whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

25. Claim 36 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al. Zhang et al. teach a DNA encoding a mouse uncoupling protein 3 which is identical in amino sequence, except for one amino acid (Ala for Val at position 260), to the protein of SEQ ID NO: 18 (column 17, claim 1; columns 9-10, SEQ ID NO:2). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make the DNA taught by Zhang et al. One of ordinary skill in the art is motivated to do this because Zhang et al. teach that the DNA encodes a mouse uncoupling protein 3. A person of ordinary skill in the art has a reasonable expectation of success at doing this because the amino acid sequence is taught by Zhang et al. The amino acid sequence taught by Zhang et al. and the instant claim differ by only one amino acid. A difference of one amino acid between the two amino acid sequences of the uncoupling protein would not be expected to give the proteins any different properties, especially since the difference is between two amino acids with similar properties. The DNAs are therefore not patentably distinct because the two proteins are not patentably distinct. Therefore the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Allowable Subject Matter

26. Claims 1, 4-12, 16, 18 and 19 are allowable over the prior art of record.

27. Claims 4-9 and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter Tung, Ph.D. whose telephone number is (703) 308-9436. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (703) 308-4216. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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